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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/610,313	07/05/2000	Susan Barnett	PP01631.101	4221

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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/610,313	BARNETT ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/6/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40 and 42-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40 and 42-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12/20/02* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Non-Final Rejection

Claims 1-40 and 42-51 are pending examination.

Applicants' traversal, the amendment to claims 1 and 29, the cancellation of claim 41, and the amendment to the specification in the paper no. filed on 10/6/03 is acknowledged and considered.

Claim Objections

Applicants are advised that should claim 29 be found allowable, claim 42 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-40 and 42-47 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-40 and 42-47 as best understood, are readable on a genus of a polynucleotide sequence encoding a polypeptide including an immunogenic HIV Pol polypeptide, wherein the

polynucleotide sequence encoding said Pol polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO: 30, 31, or 32, wherein the genus of polynucleotide sequences is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates production of a genus of a polynucleotide sequence encoding a polypeptide including an immunogenic HIV Pol polypeptide, wherein the polynucleotide sequence encoding said Pol polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO: 30, 31, or 32. The as-filed specification provides sufficient description of an immunogenic HIV Pol polypeptide set forth in SEQ ID NO: 30, 31, or 32. The as-filed specification recites that the synthetic HIV Pol polynucleotides will be capable of higher protein production compared to wild-type HIV Pol polynucleotide sequences (page 36). The specification and the art of record teach that HIV Pol comprises the enzymes reverse transcriptase (RT) and integrase (INT). The specification states, "Because synthetic HIV-1 Pol expressed the functional enzymes reverse transcriptase (RT) and integrase (INT) (in addition to the structural proteins and protease), it may be helpful in some instances to inactivate RT and INT functions (page 73)." The claims recite a structure (polynucleotide encoding an immunogenic HIV Pol polypeptide), but do not recite a function for the genus of polynucleotide sequences. In view of the phrase "HIV Pol polypeptide", the

polypeptide has to be identical to one found in an HIV in nature. The specification does not disclose how to distinguish between natural amino acid sequence and non-natural sequence that is also at least 90% identical. One skilled can envision a sequence that is at least 90% identical to the claims SEQ ID NOs., but would be unable to determine if it was an HIV sequence that was found in nature. Thus, in view of the reasons set forth above and the numerous sequences embraced by the genus, the specification does not disclose which activities correspond to the claimed genus of polynucleotides with 90% sequence identity to the claimed SEQ ID NOs: or how to distinguish between natural amino acid sequence and non-natural sequence that is also 90% identical.

It is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of polynucleotide sequences as claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or molecular structures of polynucleotide sequences that must exhibit the disclosed biological functions as contemplated by the claims.

It is not sufficient to support the present claimed invention directed to a genus of a polynucleotide sequence encoding a polypeptide including an immunogenic HIV Pol polypeptide, wherein the polynucleotide sequence encoding said Pol polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO: 30, 31, or 32. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and

which is not conventional in the art as of applicant's effective filing date. Claiming a genus of polynucleotide sequences that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of a polynucleotide sequence encoding a polypeptide including an immunogenic HIV Pol polypeptide, wherein the polynucleotide sequence encoding said Pol polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO: 30, 31, or 32 that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Applicant's arguments filed 10/6/03 have been fully considered but they are not persuasive.

Applicants argue that, "The specification describes, in detail, how Pol polypeptides are identified, for example Western Blotting, ELISA or the like and how to determine immunogenicity"; "Further, sequences of various Pol-encoding polynucleotides were known at the time of filing and are described, for example, in the Background section and references cited therein"; "The specification clearly describes how to determine percent identity as between polynucleotides or polypeptides"; "Any polynucleotide exhibiting the requisite 90% identity could then be expressed, and the polypeptide product readily tested for immunogenicity". See pages 8-14.

Applicants' arguments have been fully considered and are not found persuasive because the specification does not provide sufficient description for a genus of sequences that meets the limitations of the claims. The claimed genus encompasses polynucleotides that are yet to be discovered or synthetic polynucleotides, etc., the disclosed feature of SEQ ID NOs: 30-32 (polynucleotide encoding an immunogenic HIV Pol polypeptide) does not constitute a substantial portion of the claimed genus. The specification does not provide sufficient description for a known correlation between sequence alignment between a claimed polynucleotide sequence and a Pol-encoding polynucleotide and the activity of the encoded Pol polypeptide. For example, the specification does not provide sufficient description for one skilled in the art to determine if a polynucleotide encoding an immunogenic HIV polypeptide with 90% sequence identity to SEQ ID NOs: 30-32 meets the limitation of the claims. It is known that a single nucleotide or amino acid change can alter the function of amino acid peptide. For example, a deletion or a substitution of one amino acid or nucleotide could result in a polynucleotide with at least 90% sequence identity to SEQ ID NOs: 30-32, but not encoding a

functional immunogenic HIV Pol polypeptide. In addition, if you replace the nucleotide at each wobble position in the polynucleotide sequence of SEQ ID NOs: 30, 31 or 32, the polynucleotide sequence would not have at least 90% sequence identity to SEQ ID NOs: 30-32, but would have 100% amino acid sequence identity. There is a substantial variation between species of immunogenic HIV Pol polypeptides. Therefore, the disclosure of SEQ ID NOs: 30-32 does not provide an adequate description of the claimed genus.

Furthermore, with respect to Applicants' arguments that, "the claims clearly recite both the structure and the function of the recited polynucleotides," the argument is not found persuasive. The argument is not found persuasive because the specification does not provide sufficient description for a polynucleotide sequence encoding a polypeptide including an immunogenic Pol polypeptide, wherein the polynucleotide having at least 90% sequence identity to the sequence presented of SEQ ID NO: 30; SEQ ID NO: 31 or SEQ ID NO: 32. The claimed invention embraces a polynucleotide sequence encoding an immunogenic HIV Pol with/without RT and INT activity. There is a substantial variation between species of immunogenic HIV Pol polypeptides with/without RT and INT activity. The specification does not provide sufficient description for the claimed genus. The page (page 17, lines 1-6) cited for description of the claimed function (immunogenic) does not provide sufficient description for an immunogenic HIV Pol polypeptide. On page 17, the specification recites the definition of an "immunogenic composition" and does not provide sufficient description for a nucleotide sequence having 90% sequence identity and retaining HIV Pol activity and is immunogenic. In view of the definition of immunogenic composition in the specification (page 17), any HIV Pol polypeptide is considered immunogenic, including nucleotide sequences encoding an HIV Pol polypeptide that

do not have 90% sequence identity to the claimed SEQ ID NOs. The prior art teaches nucleotide sequences encoding an immunogenic HIV Pol polypeptide that are not 90% identical to SEQ ID NO: 30, 31 or 32. See US Patent 6,541,248 (SEQ ID NO: 2 and 5).

With respect to applicants' arguments that, "The office reliance of *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997) is misplaced," is not found persuasive. The argument is not found persuasive because the general concept of the cases is directed to possession of species does not equate with possession of genus and written description requires the specification to disclose sufficient description of the genus at the time the application was filed. This is the case here. Thus, the argument is not found persuasive for the reasons set forth above.

The declaration under 37 CFR 1.132 filed 9/8/03 is insufficient to overcome the rejection of claims 1-40 and 42-47 based upon 112 written description as set forth in the instant Office action because: for the reasons set forth above the specification does not describe the invention in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-40 and 42-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an expression cassette comprising the polynucleotide sequence set forth in SEQ ID NOs: 30, 31, or 32, does not reasonably provide enablement for a polynucleotide sequence encoding a polypeptide including an immunogenic HIV Pol polypeptide, wherein the polynucleotide sequence encoding said Pol polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID

NO: 30, 31, or 32. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The invention lies in the field of producing a composition comprising an expression cassette comprising an HIV Pol polypeptide set forth in SEQ ID NOs: 30-32 and using the composition for generating an immune response in a subject.

The specification contemplates: 1) Expression assays for the synthetic coding region of Pol, Env, and Gag-protease expression cassettes; 2) In vivo immunogenicity of Gag, Pol, and Env expression cassettes using plasmid DNA carrying the synthetic Gag, Pol, and Env expression cassette; 3) DNA immunization of non-human primates by administering intradermally, mucosally, bilaterally, intramuscularly into the quadriceps using various doses of a synthetic Pol, Env, and Gag-containing plasmid; 4) In vitro expression of recombinant alphavirus vectors or plasmid containing the synthetic Gag, Pol, and Env expression cassette; 5) In vivo immunogenicity of recombinant Sindbis replicon vectors containing Gag, Env, and Pol expression cassettes in mice by using intramuscular and subcutaneous routes.

The specification further recites that these experiments will exhibit increased potency for induction of cytotoxic T-lymphocytes (CTL) response and humoral immune response by using the Gag, Pol, and Env expression cassettes.

The specification recites, "Because synthetic HIV-1 Pol expressed the functional enzymes reverse transcriptase (RT) and integrase (INT) (in addition to the structural proteins and protease), it may be helpful in some instances to inactivate RT and INT functions (page 73)."

The as-filed specification does not provide sufficient guidance and/or factual evidence for one skilled in the art to make and/or use a sequence having at least 90% identity to any of the sequences presented as SEQ ID NO: 30, 31, or 32 other than the sequences themselves. The claims embrace a polynucleotide that encodes a polypeptide including an immunogenic HIV Pol polypeptide and wherein the sequences is at least 90% sequence identity to the sequence presented in SEQ ID NO: 30-32. The claimed invention embraces polynucleotide sequence encoding immunogenic HIV Pol with RT and INT activity retained, immunogenic HIV Pol without RT and/or INT activity. The specification teaches that HIV Pol comprises the enzymes reverse transcriptase (RT) and integrase (INT). The specification provides no guidance as to which (if any) of the amino acids may be changed while RT and INT activity are retained. The number of nucleotides in each SEQ ID NO: is at least 2457 nucleotides and thus at least 819 amino acids is encoded by each nucleotide sequence set forth in SEQ ID NOs: 30-32. The total number of 819 amino acid peptides is 1.85×10^{66}. The number of single amino acid substitutions is 15,561. The number of two amino acid substitutions is over 242,000,000. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The specification does not provide sufficient guidance and/or factual evidence that it was routine to substitute or delete at least 240 nucleotides of a 2,400 nucleotide sequence and determine which nucleotide sequences meet the functional limitation of the claims. The effects

of these changes is largely unpredictable as to which ones have a significant effect versus not. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over polypeptides of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Baker et al., Science, 294:pages 93-96, 2001); Attwood, T (*Science*, vol. 290, no. 5491, pp. 471-473, 2000); Gerhold et al., (*BioEssays*, vol. 18, no. 12, pp. 973-981, 1996); Russell et al., *Journal of Molecular Biology*, vol. 244, pp 332-350, 1994); and Wells et al., *Journal of Leukocyte Biology*, vol. 61, no. 5, pp. 545-550, 1997). Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain immunogenic HIV Pol activity, and the fact that the relationship of the sequence of a peptide and its tertiary structure (*e.g.* its activity) are not well understood and are not predictable (Ngo et al. The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), it would require an undue amount of experimentation for one skilled in the art in view of the prior art to arrive at other sequences that have at least 90% sequence identity to an immunogenic Pol polypeptide encoded by SEQ ID NOs: 30-32 and still possess HIV Pol polypeptide activity. Since it would require undue experimentation to identify other that have immunogenic HIV Poly activity, it certainly would require undue experimentation to make their corresponding DNA, and therefore, the entire scope of the claimed invention.

In conclusion, the as-filed specification and claims coupled with the state of the art at the time the invention was made only provide sufficient guidance and/or evidence to reasonably

enable making and using an expression cassette comprising the polynucleotide sequence set forth in SEQ ID NOs: 30, 31, or 32, does not reasonably provide enablement for a polynucleotide sequence encoding a polypeptide including an immunogenic HIV Pol polypeptide, wherein the polynucleotide sequence encoding said Pol polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO: 30, 31, or 32. One would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the In Re Wands Factors including the lack of guidance in the application's disclosure, the unpredictability of producing nucleotide sequences encoding an immunogenic HIV Pol polypeptide with 90% sequence identity to the claimed SEQ ID NOs.

Applicant's arguments filed 10/6/03 have been fully considered but they are not persuasive. In view of the In Re Wands Factors, the as-filed specification does not provide sufficient guidance for one skilled in the art to practice the full scope of the claimed invention.

With respect to applicants' argument that, "Applicants are under no legal obligation to teach or exemplify each and every member of a claimed genus" and "Four representative examples of sequences falling within the scope of the claims are provided in the specification" and "determining sequence identify was **utterly routine**" and "the examiner has provided no such support for the argument presented in the current rejection (pages 16-17)," the argument is not found persuasive.

The examiner acknowledges that applicants are under no legal obligation to teach or exemplify each and every member of a claimed genus. However, the court in Enzo 188 F.3d at 1374, 52 USPQ2d at 1138 states:

It is well settled that patent applications are not required to disclose every species encompassed by their claims, even in an unpredictable art. However, there must be sufficient disclosure, either through

illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed.
In re Vaeck, 947 F.2d 48, 496 & n.23. 30 USPQ2d 1438, 1445 &n23 (Fed. Cir. 1991)(citation omitted). Here, however, the teachings set forth in the specification provide no more than a "plan" or "invitation" for those of skill in the art to experiment...; they do not provide sufficient guidance or specificity as to how to execute that plan. See Fiers v. Revel. 984 F.2d.1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993); In re Wright, 999 F.2d...[1557], 1562, 27 USPQ2d...[1510], 1514. [Footnote omitted].

The claims embrace a polynucleotide that encodes a polypeptide including an immunogenic HIV Pol polypeptide and wherein the sequences is at least 90% sequence identity to the sequence presented in SEQ ID NO: 30-32. The claimed invention embraces polynucleotide sequence encoding immunogenic HIV Pol with RT and INT activity retained and an immunogenic HIV Pol without RT and INT activity. The specification provides no guidance as to which (if any) of the amino acids may be changed while RT and INT activity are retained. The specification does not provide sufficient guidance or factual evidence for a known correlation between nucleotide sequence alignment and amino acid sequence alignment. For example, the specification does not provide sufficient guidance for one skilled in the art to determine without undue experimentation if a polynucleotide encoding an immunogenic HIV polypeptide with 90% sequence identity to SEQ ID NOs: 30-32 meets the limitation of the claims. The claimed invention embraces natural sequences and recombinant sequences that could encode a non-functional/functional immunogenic HIV Pol polypeptide and the specification does not teach how to determine without further experimentation what sequences are functional. It is known that a single nucleotide or amino acid change can alter the function of amino acid peptide. For example, a deletion or a substitution of one amino acid or nucleotide could result in a polynucleotide with at least 90% sequence identity to SEQ ID NOs: 30-32, but not encoding a functional immunogenic HIV Pol polypeptide. In addition, if you replace the nucleotide at each wobble position in the polynucleotide sequence set forth in SEQ ID NO: 30, 31 or 32, the polynucleotide sequence

would not have at least 90% sequence identity to SEQ ID NOs: 30-32, but would have 100% amino acid sequence identity. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states:

> Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements, while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

The specification does not provide sufficient guidance and/or factual evidence that it was routine to substitute or delete at least 240 nucleotides of a 2,400 nucleotide sequence and determine without undue experimentation, which nucleotide sequences meet the functional limitation of the claims. On this record, it is apparent that the specification provides no more than a plan or invitation in view of the art of record exemplifying the unpredictability of making and using the claimed genus of polynucleotide sequences, for those skilled in the art to experiment with polynucleotide sequences having 90% identity to the SEQ ID NOs: 30-32 and are immunogenic and retain Pol activity as intended by the as-filed specification at the time the invention was made.

With respect to applicant's argument that, "the cases cited are not applicable (page 18)," the argument is not found persuasive. The argument is not found persuasive because Enzo 188 F.3d at 1374, 52 USPQ2d at 1138 teaches that even though the specification is not required to disclose each and every species, there must be sufficient guidance to for one skilled in the art to make and use the claimed invention as broadly claimed. This is the case here. In view of the In

Re Wands Factors, the specification does not teach one skilled in the art how to make and use the full scope of the claimed invention.

The declaration under 37 CFR 1.132 filed 9/8/03 is insufficient to overcome the rejection of claims 1-40 and 42-47 based upon 112 enablement as set forth in the instant Office action because: In view of the In Re Wands Factors, the as-filed specification does not provide sufficient guidance for one skilled in the art to practice the full scope of the claimed invention.

Furthermore, with respect to the statement that, "Also using techniques in our laboratories demonstrate that expression cassettes that include modified HIV-Pol-encoding sequences undue potent Pol-specific immune response" and "the results are summarized in Exhibit B (in zur Megede et al. (2002) J. Virol. 77(11):6197-6207)"; "the results in Exhibit B with regard to subtype B sequences are equally applicable to modified polynucleotides obtained from subtype C isolates, as claimed." The Declaration is insufficient to overcome the 112 enablement rejection because the exhibit embraces distinct materials from the materials used or contemplated in the specification. The specification is directed to making and using HIV-C Pol polypeptides and the post-filing article (Exhibit B) is directed to HIV Pol- subtype B sequences. Furthermore, Exhibit B is an article that was published in 2003 and not 2002 as stated by Dr. Donnelly.

Furthermore, with respect to the statement that, "the results in Exhibit B with regard to subtype B sequences are equally applicable to modified polynucleotides obtained from subtype C isolates, as claimed." The statement is insufficient to overcome the enablement rejection because the Exhibit is not supported by the specification because the specification does not provide sufficient guidance for how Exhibit B is equally applicable to polynucleotides obtained

from subtype C. The specification lacks sufficient guidance for which (if any) of the amino acids may be changed while RT and INT activity are retained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 48-51 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 71, 72, and 91 of co-pending Application No. 09/899,575 (SEQ ID NO: 30). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims from both applications recite an expression cassette comprising a polynucleotide sequence encoding a polypeptide including an immunogenic HIV Pol polypeptide. SEQ ID NO: 30 in the instant application is 100% identical to SEQ ID NO: 30 in application '575.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priede

Brian Whiteman
Patent Examiner, Group 1635

SCOTT D. PRIEDE, PH.D
PRIMARY EXAMINER